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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,198	12/21/2001	Merrill A. Biel	22,272-22	9166

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EXAMINER
SHAY, DAVID M

ART UNIT	PAPER NUMBER
3739	9

DATE MAILED: 02/27/2004

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/026,198	Beil
Examiner	**Group Art Unit**
I-Fy	3739

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE — 3 — MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on November 7, 2003.

☑ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 1-7, 9-16, 18-20, 22-34, + 40-52 is/are pending in the application.

Of the above claim(s)_____ is/are withdrawn from consideration.

☐ Claim(s)_____ is/are allowed.

☑ Claim(s) 1-7, 9-16, 18-20, 22-34, + 40-52 is/are rejected.

☐ Claim(s)_____ is/are objected to.

☐ Claim(s)_____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on_____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on_____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)_____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:_____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s)._____

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other_____

Office Action Summary

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-3, 5-7, 9, 11, 15, 16, 19, 20, 22-25, and 30-32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Vogel et al.

See column 11, line 8 to column 16, line 25.

Claims 1-4, 5-7, 9, 11, 15, 16, 18-20, 22-25, 30-34 and 40-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilk et al ('020) in combination with Wilk et al ('675) and Vogel et al. Wilk et al ('020) teach sterilizing medical equipment such as catheters using light applied internally or externally of the surface. Wilk ('675) teach the use of the irradiation and a sterilizing solution. Vogel teach a solution as claimed that can be used in conjunction with light to kill bacteria or to treat viral conditions. It would have been obvious to the artisan of ordinary skill to employ in the method of Wilk et al ('675), the solution of Vogel et al to sterilize the long dwelling catheters etc of Wilk et al ('020), upon which biofilms form and to employ the method of Wilk et al ('675) on other body inserted lumens such as endotracheal tubes intravenous catheters, since these are equivalent to the catheters of Wilk et al ('020) and since these are also recognized in the art as sites which require sterilization, thus producing a method such as claimed.

Claims 1, 5, 10-15, 20, and 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vogel et al in combination with Nitzan et al. Vogel et al teach a method of eradicating acellular or cellular organisms as claimed but does not teach adding the surface acting agent prior to the photosensitive material, or a plurality of photosensitizer or surface acting agents or the light dosage rate. Nitzan et al teach a method of photosensitizing cells using

a photosensitizer-surfactant mixture which will perform as claimed (The PMNP, which is made from Polymyxin B sulfate will retain some of the polymyxin B therein, and thus is considered a mixture of a plurality of surfactants) except for the specific time period between the addition of two agents and the use of benzalkonium. It would have been obvious to the artisan of ordinary skill to employ benzalkonium chloride in the solution used in the method of Nitzan et al, since this will inhibit bacterial and fungal contamination of the solution and to make the interval between the addition of two agents between one and 30 minutes since this is not critical and would allow the membranes to be permiabilized prior to addition of the dye or alternatively to employ the surfactants, dosage rate, and photosensitive agents of Nitzan et al in the method of Vogel et al, since Vogel et al specifically state the surfactants may be added, since this would improve gel properties and also to employ the photosensitize agents since this would yield a composition also useful against gram negative bacteria, as taught by Nitzan et al, thus producing a method such as claimed.

Applicant argues that Vogel et al describe an intravenous solution, which would be diluted by the blood and thus would not fulfill the concentration requirement. The examiner respectfully notes that Vogel et al also teach topical formulations (see column 13-14 "Topical Formulations"), which can include preservatives and inhibitors such as benzalkonium chloride (see Shastri et al incorporated by reference in column 14 line 33) the inhibitory concentrations being given in column 12 lines 41-50 of Vogel et al. Thus applicant's arguments are not well founded.

Applicant argues that Vogel et al is not applicable under 35 USC 102 to the current claims because Vogel et al do not describe the action of benzalkonium chloride on the organisms

to be photo dynamically treated as recited in the claims. However, since Vogel et al teach combining the benzalkonium chloride with the photosensitizer, and since Vogel et al discuss no means for a desirability of extracting the benzalkonium chloride from the photosensitizer before it is administered, the step of applying the compound of Vogel et al will inherently also apply the benzalkonium chloride as well and the surfactant will have the same effect on the cell membrane, regardless of the reason for which it was added to the compound. Thus even assuming arguendo that Vogel et al were completely ignorant of the effect of benzalkonium chloride contemplated by applicant, this effect, and thus the claimed disorienting, passing, and disruption would still inherently occur in the method of Vogel et al. Thus applicant's arguments regarding the lack of disclosure of Vogel et al are immaterial to the anticipation of the claims thereby.

Applicant then argues that there is no motivation to combine these references. The examiner cannot agree. Wilk et al ('675) undeniably teach the use of a sterilizing fluid. Vogel et al teach that the activation of the solution produces singlet oxygen species, which are lethal to viral, retroviral, and bacterial contaminants. Since the killing of such organisms provides sterilization and since Wilk et al ('675) teaches no particular sterilizing fluid, one having ordinary skill would clearly be motivated to employ the compound of Vogel et al in the method of Wilk ('675). Thus the perceived suitability of benzalkonium chloride as a sterilant is immaterial to the propriety of the combination.

Regarding the combination Nitzan et al, applicant alleges that "Neither PMNP or PMNP-DP complex causes disruption of the cell membrane," pointing to column 1 of page 94 of Nitzan et al as a basis for this statement. The examiner has found no support for this assertion in the cited passage. In fact, quite the contrary, this passage states, in pertinent parts "the Gram

negative bacteria photosensitization will be possible only be a disturbance in the cytoplasmic membrane's structure" (page 94, column 1, first full sentence) and "colisten nonapeptide and PMNP, known as membrane disorganizing agents...have been used (page 94, column 1, second full sentence). For a clearer showing of the fact that PMNP allows DP to penetrate the outer covering of the cell, applicants attention is respectfully invited to the second paragraph on page 95, column 1 of Nitzan et al: "It is clear that PMNP disturbs and disorganizes (by its action) the outer-membrane structure of the Gram negative bacteria ... without the disturbance of the outer membrane the DP cannot act on the inner membrane ... Disruption of the outer membrane structure by PMNP allows the penetration of the porphyrin and consequently enables the killing of the Gram-negative bacteria".

Applicant's arguments regarding the use of benzalkonium to improve the viscosity of a gel are not convincing, as Vogel et al teaches the use of benzalkonium in topical applications as already set forth above.

Applicants flawed interpretation of the teachings of Nitzan et al which fail to recognize the use of PMNP to access that portion of the cell which is interior to the outer membrane and the similarly flawed interpretation of teachings of Vogel et al regarding the motivation for use benzalkonium and means of administering the composition allows applicant to come to the also flawed conclusion that Nitzan et al teach away from the claimed method. Since the mixture of Nitzan et al is used to inoculate multiple solutions, it is a "multi-dose" batch. The examiner notes that Nitzan et al are experimenting with several particular strains of bacteria, thus the presence of unintended strains of bacteria, fungus, or other contaminants in the studied population would yield erroneous results. Thus Nitzan would be motivated to employ the

benzalkonium chloride as an addition to the solution. The examiner has at no time suggested that the benzalkonium chloride be substituted for any constituent of the solution of Nitzan et al. Assertions of non-obviousness predicated on the erroneous interpretation of the examiners position are not convincing.

Applicant has requested documentary proof of the presence of polymyxin – B sulfate in the PMNP solution of Nitzan et al. The examiner has included the publication to Vaara et al " Polycations sensitize enteric bacteria to antibiotics", which provides such proof.

Applicant's arguments filed November 7, 2003 have been fully considered but they are not persuasive. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to David Shay at telephone number 308-2215.

Shay/Dl

February 2, 2004

DAVID M. SHAY
PRIMARY EXAMINER
GROUP 330